

Claims

- 1 1. A method of for measuring brain activity comprising:
 2 noninvasively obtaining signals of central nervous system (CNS) activity;
 3 localizing signals to specific anatomical and functional CNS regions which
 4 participate in reward/aversion functions;
 5 correlating the signals in a reward/aversion brain region; and
 6 interpreting the correlation results.
- 1 2. The method of Claim 1, wherein the reward/aversion regions are subcortical
 2 gray, brainstem, cerebellum and frontal brain regions.
- 1 3. The method of Claim 2 wherein the brainstem region includes the spinal cord.
- 1 4. The method of Claim 3 wherein the spinal cord includes the trigeminal
 2 nucleus and the method further includes the step of non-invasively obtaining signals
 3 from the trigeminal nucleus.
- 1 5. The method of Claim 3, wherein the reward/aversion regions include at least
 2 one of the GOB, VT/PAG, NAc, SLEA, cingulate gyrus, S1, S2, thalamus, insula,
 3 cerebellum, prefrontal cortex, amygdala, hypothalamus, parahippocampal gyrus,
 4 hippocampus, entorhinal cortex, ventral pallidum, dorsal striatum, M1, M2, SMA,
 5 FEF, RVM, and brainstem subnuclei.
- 1 6. The method of Claim 1, wherein obtaining signals of CNS activity includes
 2 using a neuroimaging device wherein the signals reflect at least one of functional
 3 activation, chemical signatures, brain structure, neurotransmission, electromagnetic
 4 activity, perfusion effects and cell metabolism.
- 1 7. The method of Claim 6, wherein the neuroimaging device corresponds to one
 2 or more of a PET device, an fMRI device, an MEG device, an EEG device, a SPECT
 3 device, an IR device, a MRS device, and a functional CT device.

11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100
101
102
103
104
105
106
107
108
109
110
111
112
113
114
115
116
117
118
119
120
121
122
123
124
125
126
127
128
129
130
131
132
133
134
135
136
137
138
139
140
141
142
143
144
145
146
147
148
149
150
151
152
153
154
155
156
157
158
159
160
161
162
163
164
165
166
167
168
169
170
171
172
173
174
175
176
177
178
179
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199
200
201
202
203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228
229
230
231
232
233
234
235
236
237
238
239
240
241
242
243
244
245
246
247
248
249
250
251
252
253
254
255
256
257
258
259
260
261
262
263
264
265
266
267
268
269
270
271
272
273
274
275
276
277
278
279
280
281
282
283
284
285
286
287
288
289
290
291
292
293
294
295
296
297
298
299
300
301
302
303
304
305
306
307
308
309
310
311
312
313
314
315
316
317
318
319
320
321
322
323
324
325
326
327
328
329
330
331
332
333
334
335
336
337
338
339
340
341
342
343
344
345
346
347
348
349
350
351
352
353
354
355
356
357
358
359
360
361
362
363
364
365
366
367
368
369
370
371
372
373
374
375
376
377
378
379
380
381
382
383
384
385
386
387
388
389
390
391
392
393
394
395
396
397
398
399
400
401
402
403
404
405
406
407
408
409
410
411
412
413
414
415
416
417
418
419
420
421
422
423
424
425
426
427
428
429
430
431
432
433
434
435
436
437
438
439
440
441
442
443
444
445
446
447
448
449
450
451
452
453
454
455
456
457
458
459
460
461
462
463
464
465
466
467
468
469
470
471
472
473
474
475
476
477
478
479
480
481
482
483
484
485
486
487
488
489
490
491
492
493
494
495
496
497
498
499
500
501
502
503
504
505
506
507
508
509
510
511
512
513
514
515
516
517
518
519
520
521
522
523
524
525
526
527
528
529
530
531
532
533
534
535
536
537
538
539
540
541
542
543
544
545
546
547
548
549
550
551
552
553
554
555
556
557
558
559
560
561
562
563
564
565
566
567
568
569
570
571
572
573
574
575
576
577
578
579
580
581
582
583
584
585
586
587
588
589
590
591
592
593
594
595
596
597
598
599
600
601
602
603
604
605
606
607
608
609
610
611
612
613
614
615
616
617
618
619
620
621
622
623
624
625
626
627
628
629
630
631
632
633
634
635
636
637
638
639
640
641
642
643
644
645
646
647
648
649
650
651
652
653
654
655
656
657
658
659
660
661
662
663
664
665
666
667
668
669
670
671
672
673
674
675
676
677
678
679
680
681
682
683
684
685
686
687
688
689
690
691
692
693
694
695
696
697
698
699
700
701
702
703
704
705
706
707
708
709
710
711
712
713
714
715
716
717
718
719
720
721
722
723
724
725
726
727
728
729
730
731
732
733
734
735
736
737
738
739
740
741
742
743
744
745
746
747
748
749
750
751
752
753
754
755
756
757
758
759
760
761
762
763
764
765
766
767
768
769
770
771
772
773
774
775
776
777
778
779
780
781
782
783
784
785
786
787
788
789
790
791
792
793
794
795
796
797
798
799
800
801
802
803
804
805
806
807
808
809
810
811
812
813
814
815
816
817
818
819
820
821
822
823
824
825
826
827
828
829
830
831
832
833
834
835
836
837
838
839
840
841
842
843
844
845
846
847
848
849
850
851
852
853
854
855
856
857
858
859
860
861
862
863
864
865
866
867
868
869
870
871
872
873
874
875
876
877
878
879
880
881
882
883
884
885
886
887
888
889
890
891
892
893
894
895
896
897
898
899
900
901
902
903
904
905
906
907
908
909
910
911
912
913
914
915
916
917
918
919
920
921
922
923
924
925
926
927
928
929
930
931
932
933
934
935
936
937
938
939
940
941
942
943
944
945
946
947
948
949
950
951
952
953
954
955
956
957
958
959
960
961
962
963
964
965
966
967
968
969
970
971
972
973
974
975
976
977
978
979
980
981
982
983
984
985
986
987
988
989
990
991
992
993
994
995
996
997
998
999
1000

- 1 8. The method of Claim 4, further comprising:
2 aligning an imaging axis of an imaging device with the spinal cord of a subject
3 such that the imaging axis is aligned in a plane parallel to a spinal cord axis and
4 perpendicular to a cerebral mid-plane; and
5 obtaining images of CNS regions in the spine.
- 1 9. The method of Claim 1, wherein non-invasively obtaining signals of central
2 nervous system obtained non-invasively further comprises:
3 correcting the signals to reduce the effects of head motion;
4 transforming the signals into a uniform atomic space;
5 normalizing the transformed signals;
6 statistically mapping the normalized signal; and
7 locating the statistical maps over images reflecting at least one of: a uniform
8 atomic space, an average anatomic space, and an individual atomic space.
- 1 10. The method of Claim 1, wherein non-invasively obtaining signals of central
2 nervous system obtained non-invasively further comprises:
3 correcting the signals to reduce the effects of head motion;
4 aligning the signals with individual brain anatomy;
5 normalizing the transformed signals;
6 statistically mapping the normalized signal; and
7 locating the statistical maps over images reflecting at least one of: a uniform
8 atomic space, an average anatomic space, and an individual atomic space.
- 1 11. The method of Claim 1, wherein correlating the signals from reward/aversive
2 brain regions comprises evaluating the temporal nature of a neuroimaging signal
3 using waveform based correlation analysis (WCA).
- 1 12. The method of Claim 11, wherein data obtained from central nervous system
2 activity is segregated temporally.
- 1 13. The method of Claim 12 wherein data obtained from central nervous system
2 activity is segregated temporally into a plurality of phases.

1 14. The method of Claim 12, wherein the step of temporally segregating include
2 the step of segregating into an early phase waveform and a late phase waveform.

1 15. The method of Claim 13, wherein interpreting the results of the correlating
2 procedure further comprises correlating a plurality of pixels from regions in the CNS
3 to distinct waveforms.

1 16. The method of Claim 15, wherein the distinct waveforms correspond to at
2 least one of an early phase waveform and a late phase waveform.

1 17. The method of Claim 15, wherein interpreting the results of the correlating
2 procedure further comprises producing indices by quantifying the signals using at
3 least one of:

- 4 a spatial analysis;
- 5 a temporal analysis;
- 6 a comparison of slope analysis;
- 7 moment analysis;
- 8 laterality analysis;
- 9 synchrony analysis;
- 10 volume analysis;
- 11 power function used to generate indices;
- 12 power spectrum analysis used to generate indices;
- 13 integral analysis; and
- 14 derivative analysis.

1 18. The method of Claim 17, wherein interpreting the results of the correlating
2 procedure further comprises using one or more quantitative indices wherein at least
3 one of the one or more quantitative indices corresponds to one of:

- 4 a coordinate index from a uniform anatomic space;
- 5 a subregion index;
- 6 a subnuclear index;
- 7 a first time index T_p corresponding to a first moment of a signal response;
- 8 a second time index Δ corresponding to a second moment of a signal response;
- 9 a rate of signal change index;

- 10 an average time of response index;
- 11 a width of response index;
- 12 a tail index corresponding to a third moment of a signal response;
- 13 an R index;
- 14 an, L index;
- 15 a fractional laterally index
- 16 a correlation factor (r) index;
- 17 a volume index;
- 18 an exponent index;
- 19 an power spectrum index representing amplitudes of signal response
- 20 harmonics and subharmonics computed using a power spectrum analysis;
- 21 an index corresponding to one or more amplitudes changes computed using an
- 22 integral analysis of a signal response;
- 23 an index corresponding to a maximum rate of change of a signal response
- 24 computed using a derivative analysis of a signal response; and
- 25 an index corresponding to a time to achieve a maximum rate of change of a
- 26 signal response computed using a derivative analysis of the signal response.

- 1 19. The method of Claim 1, further comprising:
- 2 providing a known first set of indices;
- 3 measuring one or more signal responses in a subject;
- 4 generating a second set of indices by computing one or more index for each of
- 5 the one or more signal responses; and
- 6 comparing the second set of indices to the first set of indices.

- 1 20. The method of Claim 19 wherein:
- 2 the step of providing the known first set of indices, includes the step of
- 3 providing the known first set of indices to a processor; and
- 4 the step of comparing the second set of indices to the first set of indices
- 5 includes the steps of:
- 6 providing the second set of indices to the processor; and
- 7 comparing the second set of indices to the first set of indices using the
- 8 processor.

- 1 21. The method of Claim 20 wherein the processor corresponds to a neural
2 network processor.
- 1 22. The method of Claim 1, further comprising:
2 selecting an experimental process which elicits a response in one or more
3 reward/aversion regions of a subject;
4 applying a reward/aversive stimulus to the subject to illicit the response; and
5 correlating the experimental process to brain activity.
- 1 23. The method of Claim 22, wherein the experimental process further comprises:
2 (a) administering to the subject at least one of: a drug, a gene product, a
3 biopharmaceutical, a virus, a gene, one or more receptors, and a neurochemical;
4 (b) applying a stimulus to the subject; and
5 (c) measuring a brain response of the subject.
- 1 24. The method of Claim 23 further comprising measuring the response of the
2 same subject over time.
- 1 25. The method of Claim 24 wherein measuring the response of the same subject
2 over time comprises the steps of waiting a period of time and repeating steps (a) – (c).
- 1 26. The method of Claim 24 wherein measuring the response of the same subject
2 over time comprises the steps of waiting a period of time and performing the steps of:
3 (a) administering a placebo to the subject;
4 (b) applying a stimulus to the subject;
5 (c) measuring an analgesic response of the subject.
- 1 27. The method of Claim 22, wherein the experimental process comprises:
2 exposing a subject to at least one of a thermal, mechanical or chemical
3 stimulus; and
4 measuring the response of the subject to the stimulus.

1 28. The method of Claim 1, further comprising:
2 administering a treatment to the subject; and
3 correlating the treatment to brain activity.

1 29. The method of Claim 26, wherein the treatment corresponds to at least one of
2 a drug/gene product, a surgical treatment, a radiation treatment, a behavioral
3 treatment, and an acupuncture treatment.

1 The method of Claim 1 wherein the step of interpreting the correlation result
2 comprises:
3 correlating the signals from pain and reward brain regions; and
4 comparing results of the correlation to a predetermined index.

1 31. A method for determining the efficacy of a treatment corresponding to one of
2 a compound, a drug, a gene product, a virus, a gene, a receptor, a neurochemical, a
3 biopharmaceutical, the method comprising:
4 non-invasively obtaining base line signals of central nervous system (CNS)
5 activity;
6 administering a dose of the treatment;
7 localizing signals to specific anatomical and functional CNS regions
8 corresponding to a reward/aversion region; and
9 correlating the signals in the reward/aversion brain region; and
10 interpreting the results of the correlation.

1 32. The method of Claim 31, wherein the dose is a therapeutic dose.

1 33. The method of Claim 31, wherein the dose is a sub-therapeutic dose.

1 34. The method of Claim 31, further comprising producing an objective
2 determination that the administered treatment alters the experience of pain in response
3 to aversive stimuli or non-aversive stimuli.

1 35. A method of evaluating a stimulus comprising:

2 (a) measuring a plurality of indices;

- 3 (b) forming a matrix pattern with the indices;
- 4 (c) measuring a subject response to a stimulus;
- 5 (d) using the subject response to compute indices for the subject; and
- 6 (e) comparing the subject indices to the matrix pattern indices to objectively
- 7 determine the condition of the subject.

1 36. The method of Claim 35 wherein the step of measuring a response includes
2 the step of administering a mechanical, thermal or chemical stimulus to the subject.

1 37. The method of Claim 36 wherein the stimulus corresponds to one of a drug
2 and a treatment.

1 38. A system for measuring indices of brain activity comprising:
2 a central nervous system (CNS) imaging device;
3 a localization processor to map signals to specific anatomical and functional
4 brain regions;
5 a correlation processor to correlate the signals from pain and reward brain
6 regions;
7 a neural network processor.